Radiological Manifestations of β-Thalassemia

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Our Patient

- A 7 year old boy presenting in 1980 to the King Faisal Specialist Hospital in Riyadh, Saudi Arabia.

- The child presented to the hospital with severe anemia, hepatosplenomegaly, and alterations in facial morphology.

- This patient was found to have β-thalassemia major.

- The child was initially seen in April of 1980 and a splenectomy was performed in June of 1980.
Our Patient: Chest X-Ray Taken on Presentation Before Splenectomy

Findings:
- Initial trabecular and cortical thinning
- Later trabecular coarsening
- Osteopenia

Courtesy of Dr. F.M. Hall
Our Patient: Chest and Abdominal Plain Films Following Splenectomy

- Absence of the Spleen
- Vertebrae show bone-in-bone appearance
- Impaired ossification at the ilium-ischium-pubic interface

Courtesy of Dr. F.M. Hall
Our Patient: Plain Films of the Hands

Normally the red marrow is restricted to central flat bones

Courtesy of Dr. F.M. Hall
Our Patient: Plain Film of the Skull

Paranasal Sinuses (Except Ethmoid) Filled with Marrow

 Courtesy of Dr. F.M. Hall
Radiological Findings in Untreated β-Thalassemia

- The first published description of β-thalassemia in 1927 by Cooley and colleagues, noted the bone changes as characteristic of the disease.

- Many of these findings can occur in other marrow infiltrative/expansive diseases (i.e. SCD, Gaucher, leukemias, mets, etc.), but they generally occur to a greater extent in untreated β-thalassemia due to the extensive degree of marrow expansion (can often be up to 15-30 fold increased).

- The marrow expansion destroys medullary trabeculae with initial cortical and trabecular thinning and subsequent trabecular coarsening. As a result, the bones become weak and can easily fracture.
Hemoglobin is Only Stable as a Tetramer of Two α- and Two β-Globin Polypeptides

Adapted from: http://en.wikipedia.org/wiki/Hemoglobin
A Review of the Pathophysiology of β-Thalassemia

Adapted from:
Toxicity Due to Precipitates of \( \alpha \)-Globin Lead to Ineffective Erythropoiesis

Ineffective Erythropoiesis

- BFU-E
- CFU-E
- Proerythroblast
- Erythroblast
- Reticulocyte
- Erythrocyte
Ineffective Erythropoiesis and Expansion of Erythroid Progenitors

Normal Erythropoiesis:

Ineffective Erythropoiesis:
The Resulting Erythroid Hyperplasia Leads to Marrow Expansion & Extramedullary Hematopoiesis

Companion Patient #1: Erythroid Hyperplasia Leads to “Cobwebbing” and a Course Trabecular Pattern

Also Notice Gallstones, Which Occur Due to Elevated Unconjugated Bilirubin

Adapted from: Tyler et al., Clin Radiol. 2006 Jan;61(1):40-52
Our Patient: Skull Findings

Diploic Space Widening

Courtesy of Dr. F.M. Hall
Companion Patient #2: Skull Vault Marrow Expansion of Diploic Space

T1-weighted MRI (Saggital Section)

Adapted from: Tyler et al., Clin Radiol. 2006 Jan;61(1):40-52
Companion Patient #3: Extramedullary Hematopoiesis in Untreated β-Thalassemia

Can see expansion into spleen, liver, and potentially paraspinal masses as in this patient.

Adapted from: Tyler et al., Clin Radiol. 2006 Jan;61(1):40-52
Treatment of β-Thalassemia

While 95% of patients with β-thalassemia live in the developing world and don’t receive adequate treatment, we can currently treat this disease by regular transfusions and iron-chelation in patients with access to care.

The major chelator for iron has been desferrioxamine (DFX). Currently newer iron chelators (including orally bioavailable ones like deferasirox) are available, though there is limited experience with their use.
Companion Patient #4: Skeletal Dysplasia Due to DFX Treatment

Metaphyseal Bands & Growth Arrest Lines

Adapted from: Tyler et al., Clin Radiol. 2006 Jan;61(1):40-52
In Addition to Rickets-Like Bone Changes, There is a Reduced Growth Velocity With DFX Therapy

Companion Patient #5: Even with Iron Chelation, Iron Deposition Becomes a Major Problem

Abdominal Section Through Liver with T2* MRI (Iron is Low Signal Here)

Adapted from: http://emedicine.medscape.com/article/369012-imaging
Excellent Quantitative Assessment of Iron Burden by T2* MRI Methods

Adapted from:
Could better and more effective treatments for β-thalassemia be developed?
Reversing the Fetal-to-Adult Hemoglobin Switch to Develop Better Therapies for β-Thalassemia

Potential to Develop Better HbF-Inducing Therapies by Targeting the Major Regulator of the Hemoglobin Switch, BCL11A

Summary

- We illustrated the skeletal alterations that can be seen on plain films in β-thalassemia.

- We explored the pathophysiology of this phenomenon and touched on other pertinent radiological findings (i.e. extramedullary hematopoiesis).

- The radiologic changes seen with chronic iron chelation were discussed.

- We mentioned the use of modern MRI methods (T2*) to quantitate iron burden.

- Finally, we touched on potential new therapeutic avenues that could ameliorate β-thalassemia.


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